REMARKS

Status of the Application

Claims 14, 25-38 and 40-41 were under current consideration, and were rejected. Claims 14, 25-41 are hereby canceled; claims 1-13, 15-24 were canceled previously. Claims 42-50 have been added.

The newly added claims do not add or constitute new matter. Support for the newly added claims may be found throughout the specification, such as, for example, at page 10, line 26 through page 15, line 3, at page 17, line 22 through page 26, line 2, and at page 50, line 24 though page 51, line 15, of the specification, and Table 1. As such, no new matter has been added by this amendment.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the cancellation of claims is made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Applicants respectfully request reconsideration of the application in view of the amendments to the claims, and remarks made herein.

Requirement for Restriction

In response to the Examiner's requirement for restriction of the claims, Applicants hereby confirm the election made by telephone, without traverse, of Invention I, claims 14, 25-38 and 40-41, drawn to a transgenic mouse comprising a disruption in an endogenous RPTPB gene, a method of producing the same mouse, and cells comprising a disruption in an endogenous RPTPB, classified in classes 800, 800 and 435, subclasses 18, 21, and 325.

Sequence Compliance

The Examiner has asserted that the instant application fails to comply with the requirements of 37 CFR 1.821 through 1.825, because the sequence disclosed in Figure 2A was not described in the sequence listing submitted with the application as filed. The Applicant submits that the sequence described in Figure 2A is identical to the sequence disclosed as SEQ ID NO:1 in Figure 1 and in the original sequence listing, and thus contend that the sequence has been included in the sequence listing filed.

The Applicant has amended Figure 2A to include the inadvertently omitted sequence identifier. New Figure 2A with the amendment incorporated therein is attached herewith.

The Applicant contends that a new sequence listing is not required. Applicants originally filed a sequence listing on December 4, 2001 with the original application, which contains the sequences disclosed in SEQ ID NO:1 through SEQ ID NO:3, and no additional sequences have been disclosed not encompassed by the sequence listing. As the sequence described in Figure 2A, to which the Examiner refers in the instant Office Action, is included in the sequence listing originally filed (SEQ ID NO:1), and in light of the amendment to Figure 2A to more clearly identify the sequence, the Applicants believe the application is now in full compliance with the requirements of 37 CFR 1.821 through 1.825.

Objection

The objection to claim 40 as being dependent on a non-elected claim is overcome in light of cancellation of the claim. Applicants request withdrawal of this objection.

Rejection under 35 U.S.C. § 101

Non-Statutory Subject Matter

The Examiner has rejected claim 40 under 35 U.S.C. § 101 as being drawn to non-statutory subject matter. Claim 40 has been canceled.

Specifically, the Examiner has asserted that the scope of the claim directed to a murine embryonic stem cell comprising a disruption in a RPTPB gene can be interpreted to read on a mouse or rat cell *in vivo* comprising a naturally occurring disruption. Applicants traverse the rejection. However, the rejection is no longer relevant in light of the cancellation of claim 40.

Utility

The Examiner has rejected claims 14, 25-38 and 40-41 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well-established utility. Applicants respectfully traverse the rejection.

Claims 14, 25-38 and 40-41 have been canceled. Pending claims 42-50 are drawn to methods of identifying agents capable of modulating activity of RTPTB, its gene expression or a phenotype, by comparing the physiological response of a transgenic mouse having a disruption in the RTPTPB gene with that of a control mouse, where a difference in the physiological response between the transgenic mouse and the control mouse is an indication that the agent is capable of

modulating activity of RPTPB, gene expression or a phenotype. The physiological response may be a change in survival rate, rate of lethality, development, vascular development or hematopoiesis. The phenotype may be a developmental abnormality, increased incidence of lethality, reduced vascular development or reduced hematopoiesis.

It is submitted that these screening methods satisfy the utility and enablement requirements of sections 101/112 as one skilled in the art would immediately recognize the use of such methods. As the rejections were directed to claims covering the transgenic mouse, Applicant submits that the rejections are rendered moot as to the method of use claims.

Rejection under 35 U.S.C. § 112, first paragraph

Utility/Enablement

The Examiner has rejected claims 14, 25-38 and 40-41 under 35 U.S.C. § 112, first paragraph, because one skilled in the art would allegedly not know how to use the claimed invention as a result of the alleged lack of either a specific or substantial asserted utility or a well-established utility for the reasons set forth in the utility rejection. Applicants respectfully traverse the rejection. However, this rejection was addressed above in response to the utility rejection under 35 U.S.C. § 101. Applicants submit that this rejection has been overcome by the cancellation of claims. Therefore, Applicants respectfully request withdrawal of the rejection.

Enablement

The Examiner further rejected claims 14, 25-38 and 40-41 on grounds of enablement. Specifically, the Examiner raised the following issues of enablement with respect to these claims: (1) the claims encompass transgenic animals and methods requiring the use of embryonic stem cells, which technology was generally limited to the mouse system at the time of filing; (2) the term murine encompasses rats (and gerbils), which is not enabled due to the limitations of ES cell technology; (3) the claims fail to require germline transmission of the genetic disruption, and therefore read on a single cell without a phenotype or a chimeric animal with an unpredictable phenotype; and (4) the specification allegedly fails to provide guidance correlating to a phenotype for some of the mice encompassed by the claims, including heterozygous mice or chimeric mice.

Applicants submit that the enablement rejection has been overcome by the cancellation of claims. As the pending claims relate to methods of identifying agents capable of modulating an activity of RTPTB, its gene expression, or a phenotype, which are described and enabled by the specification, this rejection is no longer relevant. More particularly, the newly added claims

overcome the issues of enablement relating to unpredictability of a phenotype, limitations of ES cell technology, germline transmission of the gene disruption, and use of the term murine. Applicants submit that the pending method of use claims are patentable and fully meet the enablement requirements set forth in the first paragraph of 35 U.S.C. § 112.

Rejection under 35 U.S.C. § 102

The Examiner has rejected claims 14, 25-38 and 40-41 under 35 U.S.C. § 102(a) as being anticipated by Harroch *et al.* (2000, *Mol Cell Biology,* Vol. 20, No. 20, pages 7706-7715). Applicants respectfully traverse the rejection.

The Examiner has cited Harroch as teaching a mouse comprising a homozygous disruption in an RPTPB gene, and has alleged that the reference anticipates all of the instant claim limitations. Applicants respectfully point out that Harroch failed to identify any phenotype resulting from disruption of the RPTPB gene ("These RPTPß-/- mice are viable and fertile and showed no gross anatomical alterations." See page 7707, column 1).

To anticipate a claim, the reference must teach every element of the claim. "**A claim is anticipated [under §102] only if each and every element as set forth in the claim is found**, either expressly or inherently described, **in a single prior art reference**." MPEP §2131 *citing* (Verdegaal Bros. V. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)).

Rejected claims 14, 25-38 and 40-41 have been cancelled. Applicants submit that Harroch fails to teach each and every limitation recited in the pending claims. As discussed above, pending claims 42-50 are drawn to methods of identifying agents capable of modulating an activity of RTPTB, its gene expression or a phenotype, by comparing the physiological response of a transgenic mouse having a disruption in the RTPTPB gene with that of a control mouse, where a difference in the physiological response between the transgenic mouse and the control mouse is an indication that the agent is capable of modulating activity of RPTPB, gene expression or a phenotype. The physiological response may be a change in survival rate, rate of lethality, development, vascular development or hematopoiesis. The phenotype may be a developmental abnormality, increased incidence of lethality, reduced vascular development or reduced hematopoiesis. The Harroch reference fails to teach any method of identifying agents, in particular the methods recited in the pending claims. More particularly, in light of the failure of Harroch to identify any of the above noted phenotypes, the reference does not teach a method for

identifying agents capable of modulating these phenotypes nor affecting physiological changes associated with such phenotypes. Therefore, Harroch cannot anticipate the presently claimed methods.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-741.

Respectfully submitted,

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AMENDMENTS TO THE DRAWINGS

Amendment to Figure 2A

Please replace originally filed Figure 2A with replacement Figure 2A attached herewith, labeled "Replacement Sheet".

Description of the Amendment

The amendment to Figure 2A is merely the addition of the sequence identifier at the end of the sequence disclosed therein (SEQ ID NO:1). The amendment does not add or constitute new matter, and is completely supported by the application as originally filed.